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EXAMINER

MEHTA, ASHWIN D

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 12/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

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Office Action Summary

Application No.

09/936,011

Applicant(s)

JONARD ET AL.

Examiner

Ashwin Mehta

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-12 and 14-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-12, 14-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10092003. 6) ☐ Other: _____

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. The objections to claims 1-7 and 9-22 are withdrawn, in light of the claim amendments or cancellations.
3. The rejection of claims 1-22 under 35 U.S.C. 112, 2nd paragraph, is withdrawn, in light of the claim amendments or cancellations.

Information Disclosure Statement

4. The listing for Xu et al., Plant Cell Reports, Vol. 15, pages 91-96 (1995), in the IDS submitted October 6, 2003 has been lined through because a copy of the reference was not received.

Specification

5. The specification remains objected to for failing to comply with 37 CFR 1.74, which requires that there be a brief description of the drawings. Applicants are required to insert a section into the specification titled, "Brief Descriptions of the Drawings," or a similar title, and which contains brief descriptions of the drawings. New matter must be avoided.

Claim Objections

6. Claim 8 remains and claims 1 and 15 are objected to because of the following informalities:

Claim 8 remains objected to for the term "foreigner" in line 2 should be --foreign--.

Appropriate correction is required.

In claim 1: the term "transplants" in line 1 should be --transgenic plants--.

In claim 15: the article "a" in line 4, before "SEQ ID NO: 3," should be deleted.

Claim Rejections - 35 USC § 112

7. Claims 1, 2, 4, 5, 7-12, 14-25, 27-29, 31, and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1: the recitation, "similar plant species" in line 14 renders the claim indefinite. It is not clear what plant species are considered to be "similar" to the transgenic plant species. It is suggested that "similar plant" be replaced with --plant of the same--.

Further in claim 1: the recitation, "such TGB2 sequence" in the last line renders the claim indefinite. It is not clear what exactly is meant or encompassed by "such." It is suggested that "without such TGB2 sequence" be replaced with, --that does not contain said nucleotide construct--.

Further in claims 1, 2, 11, 12, and 15: the recitation, "or its complement or its corresponding RNA sequence" renders the claims indefinite. Parent claims 1 and 11 indicate that the nucleotide construct expresses a TGB2 protein whose functional activity has been

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changed. The claims also indicate that the nucleotide sequence can have homology to the complement or corresponding RNA of SEQ ID NO: 1. However, the complementary sequence does not encode the TGB2 protein whose functional activity has been changed, and therefore cannot express it.

In claims 23 and 27: the recitation, "variant sequence of SEQ ID NO: 1 due to redundancy of code" in line 2 renders the claims indefinite. The paragraph bridging pages 10-11 states, "The variants of the wild-type nucleotide sequence (SEQ ID NO. 1) comprise insertion, substitution or deletion of nucleotides encoding the same or different amino acid(s)". However the term "comprise" is open language, and indicates that variants can comprise something else. Further, it is not clear what code is being referred to by "redundancy of code." The claim does not make clear that the "code" is the genetic code. Further, if the code is referring to the genetic code, then the encoded TGB2 protein is not a mutant protein that has at least one amino acid change compared to wild-type TGB2, as required by parent claims 1 and 11. This also renders claims 23 and 27 indefinite.

In claims 24 and 28: the recitation, "a modification is made in the hydrophilic region" renders the claims indefinite. It is not clear what is meant by "modification." Parent claims 1 and 11 indicate that at least one deletion, insertion, or substitution is to be made to SEQ ID NO: 1, resulting in a mutant TGB2 protein that has least one amino acid change. However, it is not clear if "modification" encompasses other types of changes, such as glycosylation.

Further in claims 24 and 28: the claims indicate that a modification is to be made to the hydrophilic region of SEQ ID NO: 1, downstream of the N-terminal hydrophobic domain. However, SEQ ID NO: 1 is a nucleotide sequence, not an amino acid sequence.

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In claims 25 and 29: the recitation, "wherein amino acids in said hydrophilic region are substituted" renders the claims indefinite. It is not clear if the recitation is indicating that all of the amino acids in the hydrophilic region are to be substituted.

In claim 29: there is insufficient antecedent basis for the recitation, "said hydrophilic region" in the claim or the claim from which it depends.

8. Claims 1, 2, 4, 5, 7-12, 14-22 remain and claims 23-25, 27-29, 31, 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record stated in the Office action mailed March 24, 2003. Applicants traverse the rejection in the paper filed September 24, 2003. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that amended claims 1-12 and 14-22 no longer recite all group I viruses and include specific sequence identifiers, and that sufficient written description has been accordingly provided (response, page 7, last full paragraph).

However, the specification does not describe any nucleotide sequences that encode a TGB2 protein whose functional activity has been changed and which has at least one amino acid change compared to wild type TGB2 of BNYVV, except for the nucleotide sequence set forth in SEQ ID NO: 3 and those differing therefrom due to genetic code degeneracy, and which inhibits the movement of BNYVV in transgenic plants that express it. The specification does not

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correlate other changes that can be made to the structure SEQ ID NO: 1 such that it will prevent BNYVV movement in plants. The specification admits that other mutant nucleotide sequences besides SEQ ID NO: 3 were also produced. However, none of their sequences are described, and none of them prevented BNVYY movement in transgenic plants expressing the sequences (specification, page 12). Further, SEQ ID NO: 3 differs from SEQ ID NO: 1 in only 6 nucleotides substitutions, and share much greater identity than 80%. Sequences that differ from SEQ ID NO: 1 by 70% have differences in 107 nucleotides, by deletion, insertion, or substitution, which is in stark contrast with the 6 nucleotide substitutions in SEQ ID NO: 3.

Further, if the mutated sequence of new claims 23 and 27 differs from SEQ ID NO: 1 due to genetic code redundancy (see the indefinite rejection above), then the claim encompasses expressing the wild type TGB2 protein in transgenic plants. However, the specification does not describe a method to make BNYVV resistant transgenic plants by expressing the wild type BNYVV TGB2 protein.

9. Claims 1, 2, 4-12, 14-21 remain and claims 22-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record stated in the Office action mailed March 24, 2003.

Applicants traverse the rejection in the paper filed September 24, 2003. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that amended claims 1-12 and 14-22 no longer recite all group I viruses and include specific sequence identifiers, and that the claims as amended are fully enabled (response, page 8, 1st full paragraph).

However, the specification does not enable nucleotide sequences encoding mutant BNYVV TGB2 proteins whose functional activity is changed and which inhibit the movement of BNYVV when expressed in transgenic plants, other than the sequence of SEQ ID NO: 3 and those that differ therefrom due to genetic code degeneracy. No guidance is provided concerning other amino acids of the protein encoded by SEQ ID NO: 1 that can be changed that would result in a protein having the same properties as that encoded by SEQ ID NO: 3. As discussed in the last Office action, the specification admits that other mutant sequences were produced, but did not inhibit movement of BNYVV in transgenic plants, or otherwise increases the resistance of the transgenic plants to BNYVV. No guidance is provided at all as to the other amino acid sequences of the protein encoded by SEQ ID NO: 1 that can be changed. Given that Applicants themselves apparently tried and failed to produce other mutant TGB2 proteins, undue experimentation would be required by one skilled in the art to produce other mutant TGB2 proteins that can be used in the claimed method. Further, SEQ ID NO: 3 differs from SEQ ID NO: 1 due to 6 nucleotide substitutions. In contrast, dozens of other changes to the sequence of SEQ ID NO: 1 are encompassed by nucleotide sequences having only 70% homology to SEQ ID NO: 1. The specification does not teach a single such sequence.

Further, new claims 23 and 27 could still encompass increasing the BNYVV resistance of transgenic plants by expressing SEQ ID NO: 1, which could encode a wild type TGB2 protein

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(see the indefinite rejection above). However, the specification on page 12 teaches that only plants expressing SEQ ID NO: 3 inhibited the movement of BNYVV in the transgenic plants.

The claim amendments and Applicants' arguments also do not address the issue, regarding claim 20, that one skilled in the art would discern any effect of BNYVV resistance on the claimed plant due to expression of the transgenic mutant TGB2 sequence, as the host plant apparently already has natural resistance against it. It is not clear how discern that the resistance is due to the transgenic sequence, since the non-transgenic plant already is resistant to BNYVV.

Furthermore, the specification does not teach a method for making transgenic plants resistant to BNYVV that comprises transforming a plant cell with a DNA sequence of the complement, or a DNA of the corresponding RNA sequence, of the nucleotide sequence having at least 70% or 80% homology to SEQ ID NO: 1. Such a method would express the antisense sequence of the nucleotide sequence that is homologous to SEQ ID NO: 1. The only method taught in the specification involves expressing the protein encoded by SEQ ID NO: 3. No antisense-mediated method is taught.

Claim Rejections - 35 USC § 103

10. Claims 1, 2, 4, 5, 7-12, 14, 16-19, 21, 22 remain and claims 25, 28, 29, 31, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beck et al. "'94" (Proc. Natl. Acad. Sci., 1994, Vol. 91, pages 10310-10314) in combination with Saito et al. (Arch. Virol., 1996, Vol. 141, pages 2163-2175), Bouzoubaa et al. (J. Gen. Virol., 1986, vol. 67, pages 1689-1700), Beck et al. "'91" (Virology, 1991, Vol. 183, pages 695-702), Hall et al. (WO 95/10178), Urwin et al. (Plant J., 1995, Vol. 8, pages 121-131), and Landsman et al. (Mol. Gen. Genet., 1988, Vol. 214,

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pages 68-73), for the reasons of record stated in the Office action mailed March 24, 2003.

Applicants traverse the rejection in the paper filed September 24, 2003. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that Beck '94 do not teach BNYVV and do not provide any expectation of success of the method as applied to BNYVV, and assert that the Examiner supposedly acknowledged that the relevant art is unpredictable (response, page 8, last full paragraph).

It is not clear to the Examiner what Applicants are referring to when stating that the unpredictability of the relevant art was acknowledged. The Examiner made no such statement in the rejection. Regarding the expectation of success with BNYVV- this is supplied by the combination of the references, as discussed in the rejection.

Applicants also argue that Saito and Bouzoubaa disclose nothing about a method for making a plant resistant to BNYVV by expression of a mutant TGB2 protein; that Beck '91 only teaches a mutated TGB2 in the context of white clover mosaic virus, that plant are inoculated, rather than transformed, with RNA in Beck '91, and that Beck '91 is a study of the gene's activity, and is not a disclosure of a transgenic plant; that Hall provides no teaching that would motivate one of skill in the art to mutate SEQ ID NO: 1 specifically to introduce the sequence into a plant such that it would provide resistance against rhizomania; and that Urwin only discloses use of the CaMV 35S promoter in tomato plants, not sugar beet, and more specifically in the context of a method of making a sugar beet resistant to BNYVV through expression of a mutated TGB2 protein (response, page 9, 1st-4th full paragraphs).

However, Applicants are attacking the cited references individually, not in combination. One cannot show nonobviousness by attacking references individually where the rejections are

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based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The rejection as presented in the previous Office action discusses how the combination of the references renders the claimed invention obvious. Beck et al. '91 and Beck et al. '94 teach that the family of viruses that white clover mosaic virus and BNYVV belong to share conserved domains in their TGB2 protein sequences. Applicants argue that Beck et al. '91 do not teach transformed plants. However, the expression of a mutated TGB2 protein in transgenic plants, and that the mutations are in conserved amino acids in the hydrophilic domain and are substitutions with alanine, is taught by Beck et al. '94. Applicants argue that Hall et al. provides no teaching of mutating SEQ ID NO: 1, but this reference was obviously cited for the teaching of a sugar beet transformation method. Applicants argue that Urwin only teaches use of the CaMV 35S promoter in tomato plants. However, this promoter has been and remains one of the most widely used, if not the most widely used, promoter in transgenic plants of all types, including at the time the instant invention was made. Further, as discussed in the previous Office action, the choice of promoter would have depended on one's desired end, and amounts to an optimization of process parameters. Furthermore, it is not necessary that a reference actually suggest changes that Applicants made. Having established the knowledge of the wide spread use of the CaMV 35S promoter was in the art, a conclusion of obviousness from common knowledge and common sense of the person of ordinary skill in the art, without any specific hint or suggestion in a particular reference, can be relied upon. See *In re Bozek*, 416 F.2d 1385, 1390, 163 USPQ 545, 549 (CCPA 1969). Even further, not all of the claims are limited to only transgenic sugar beet plants. See *In re Lindner*, 173 USPQ 356 (CCPA 1972) and *In re Grasselli*, 218 USPQ 769 (Fed.

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Cir. 1983) which teach that the evidence of nonobviousness should be commensurate with the scope of the claims.

11. Claims 23 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baulcombe (Plant Cell, 1996, Vol. 8, pages 1833-1844), Saito et al. (Arch. Virol., 1996, Vol. 141, pages 2163-2175), Bouzoubaa et al. (J. Gen. Virol., 1986, Vol. 67, pages 1689-1700), Hall et al. (WO 95/10178), Urwin et al. (Plant J., 1995, Vol. 8, pages 121-131), and Landsman et al. (Mol. Gen. Genet., 1988, Vol. 214, pages 68-73), for the reasons of record stated in the Office action mailed March 24, 2003 under item 7 for claims 1-22. Applicants traverse the rejection in the paper filed September 24, 2003. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that Baulcombe contains no particular reference or teaching that would motivate one of ordinary skill in the art to prepare a mutant TGB2 sequence and use it to make BNYVV resistant transgenic plants, and that the other references do not cure the deficiencies of Baulcombe (response, page 10, 2nd full paragraph). However, claims 23 and 27 can read on expression of a nucleotide sequence that differs from SEQ ID NO: 1 by genetic code redundancy (see the indefinite rejection above). A mutant TGB2 protein in this case would not be expressed.

Summary

12. Claims 1, 2, 4-12, 14-32 are rejected.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this

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application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

December 4, 2003



Ashwin D. Mehta, Ph.D.
Primary Examiner
Art Unit 1638